REMARKS

Claims 1-13 were examined; claims 14-19 were withdrawn from consideration. Claim 4 was objected to. Claims 1-13 were rejected under 35 USC §112, second paragraph. Claims 6 and 13 were rejected under 35 USC §112, first paragraph. Claims 1-3, 5, and 7-12 were rejected under 35 USC 102(b) as being anticipated by Karr. Claims 1-13 were rejected under the ground of nonstatutory obviousness double patenting in view of claims 1-33 of commonly owned US patent 6,950,028 and claims 1-25 of commonly owned application 10/824,709 (since issued as US patent 7,102,526).

Re-examination and reconsideration of the claims, as amended, is respectfully requested.

Brief review of the specification:

Applicant believes that before proceeding with the response, a review of some of the key elements from the specification will be useful.

"The present invention consists of a time-temperature indicator device that has at least one parameter set to warn when a therapeutic protein drug has had a thermal history associated with increased risk of unwanted immunological activity. The indicator device is designed to remain with the drug as the drug travels throughout different links of the cold chain. In a preferred embodiment, the indicator device remains associated with the therapeutic protein from the time of manufacture up until the final few minutes before the drug is used. In alternate forms of the invention, additional parameters, including motion, light, and turbidity may also be monitored. Novel methods for determining therapeutic protein time-temperature immunological risk parameters, and programming or adjusting the indicator device, are also disclosed". [Abstract]

"At least one of the parameters of the time-temperature indicator devices of the present invention is determined by tests for immunological stability, which is distinct from functional stability. The final stability of the therapeutic protein is determined based on a

function that incorporates both the time and temperature profile required to maintain functional activity, and the time and temperature profile necessary to avoid the production of therapeutic protein degradation products that are typically associated with risk of unwanted immunological activity." [Specification paragraph 26]

"Since the immune system is extremely sensitive, only a small amount of degradation, on the order of a few percent or less of the total material, may trigger an unwanted immune response. Thus often, such degraded material, although now immunologically unacceptable, may otherwise still perform adequately in all other therapeutic areas. For example, a therapeutic protein may lose from <1% to 10% of its protein to a degraded and potentially antigenic form, yet not show any significant change in functional activity, since 90 to 99% of the material would still be unaffected. Thus typically the immunological stability of a therapeutic protein is affected before the functional stability of the protein is affected. That is, a protein tested and released to strict immunological stability standards will typically have a restricted time and temperature stability profile, relative to proteins tested and classified only by standard (and non-immunological) functional stability criteria." [Specification paragraph 27]

The present invention has two aspects. The first aspect of the invention is based upon the concept of using "immunological stability" as one of the primary criteria for determining the shelf life and storage conditions of therapeutic proteins, and using this data as a key input into the final assessment of the therapeutic's final "acceptable stability" profile. Here, the utility of using immunological stability for shelf life dating is proposed, along with various methods to determine immunological stability shelf life and storage conditions. [Specification paragraph 40]

In the second aspect of the invention, indicator devices are disclosed that continually monitor a therapeutic protein's storage conditions, and warn users when the immunological stability profile of the therapeutic has been exceeded, and can also warn when other time-temperature storage criteria have been exceeded. [Specification paragraph 41]

In other words, the application teaches a novel device and method of warning when a therapeutic protein drug has had a thermal history that may cause the drug to generate an unwanted immune response (become antigenic, exhibit immunological risk) when the drug is administered to a patient.

Claim objections:

Response to section 3: The objection of claim 4 under 37 CFR 1.75c that *"claim 4 includes a limitation of a therapeutic protein drug and the instant claims are not drawn to a therapeutic protein drug but a time-temperature indicator device ... "the claim does not further limit its parent claim 1"* is respectfully traversed in part and overcome in part.

Claim 4 is a dependent claim to claim 1. Claim 1 teaches a *"device for monitoring a therapeutic protein drug."*[Emphasis added] Applicant respectfully traverses the objection of claim 4 on the basis that claim 4 does further limit its parent claim. Specifically claim 1 (prior to amendment) previously taught a time temperature indicator for monitoring any therapeutic protein drug. Claim 4 further limited the teaching to time-temperature indicators for monitoring a therapeutic protein drug that does not normally provoke an immune response and which is not a vaccine. Thus claim 4 did, in fact, further limit previous (prior to amendment) claim 1 to a smaller category of drugs.

Since examiner did not otherwise find grounds to reject claim 4, and further suggested that one option to proceed was to "rewrite the claim(s) in independent form" applicant has taken examiner's suggestion. Since, as discussed in many places in the specification, the purpose of this device is to warn when an immunological risk threshold has been passed (i.e. when a previously non-immunogenic drug has now become immunogenic), applicant is willing to incorporate the key limitation of objected claim 4: *"in which the therapeutic protein drug does not normally provoke an immune response, and in which the therapeutic drug is not a vaccine"* into all of the application's independent claims (claims 1, 7, 21, and 22). As a result, all pending claims in this response now are variants

of objected-to claim 4, rewritten in independent form, and correcting the other claim drafting errors noted by examiner.

In this case, for internal claim consistency, better clarity, and to avoid antecedent basis issues these claim 4 limitations were slightly rewritten as: *"in which said therapeutic protein drug does not normally provoke an immunological reaction in the absence of said structural or chemical alterations, and in which said therapeutic protein drug is not a vaccine;"*. These claim 4 limitations were then placed directly below the limitations in independent claims 1, 7, 21, and 22 that teach immunological risk thresholds.

Thus applicant respectfully submits that by incorporating the claim 4 limitations, claims 1-3, 5-13, and 20-23 can now all be viewed as variants of objected-to claim 4, and thus, pending correction of other drafting deficiencies noted by examiner, should be allowable. Amendments to correct these other drafting deficiencies will be addressed in the following response to office action sections 5-16.

Since, as will be discussed, amended independent claims 1, 7, 21, and 22 now incorporate the limitations of original objected-to claim 4, original claim 4 has been canceled because it is now redundant.

Rejections under 35 USC §112, second paragraph

Response to section 5:

Applicant has overcome examiner's rejection that "the structure which goes to make up the device must be clearly and positively specified" by amending independent claims 1 and 7 to more clearly teach that the device is an "indicator comprising: a time-temperature integrator with means to integrate time and temperature, an indicator output means, and a time-temperature indication parameter setting means;".

The "means to integrate time and temperature" limitations, as well as the "indicator output means" limitations of this amendment find support in specification paragraphs 54-56.

Paragraph 54 discusses devices produced from chemically based integrating time temperature indicators. Paragraph 55 incorporates copending application 10/634,297 (now US patent 6,950,028), which discloses a specific type of electronic integrating time-temperature indicator. Paragraph 56 discusses the work of Sjoholm et. al. (WIPO WO 0125472A1), which discloses a third type of hybrid chemical-electronic integrating time-temperature indicator with an RFID output.

The time-temperature indication parameter "setting" means limitation finds support in the abstract of the specification: *"The present invention consists of a time-temperature indicator device that has at least one parameter set to warn when a therapeutic protein drug has had a thermal history associated with increased risk of unwanted immunological activity."*[emphasis added]

The "setting" limitation also finds support in specification paragraphs 25, 26, 28, 87, 131-133, and elsewhere:

"The present invention consists of a time-temperature indicator device that has at least one parameter set to warn when a therapeutic protein drug has had a thermal history associated with increased risk of unwanted immunological activity." [Paragraph 25, emphasis added]

"At least one of the parameters of the time-temperature indicator devices of the present invention is determined by tests for immunological stability"; [Paragraph 26, emphasis added]

"Such risks can be mitigated by carefully characterizing the environmental conditions likely to produce antigenic protein degradation products, and programming this data into

indicator devices that can remain associated with the biotherapeutic throughout its product life." [Paragraph 28, emphasis added]

Response to section 6:

The rejection that *"the claims do not disclose what components are required for the time temperature device"* is respectfully traversed in part and overcome in part. As amended, claim 1 now teaches that the method employs a device that contains *"means to integrate time and temperature, an indicator output means, and a time-temperature indication parameter setting means;"* This means plus function claims language is allowed under 35 USC 112, sixth paragraph.

Response to sections 7 and 8:

Examiner's rejection that *"it is unclear who is performing these activities. One interpretation is that a practitioner performs the activities. Another interpretation is that the device itself performs the activities, for purposes of this examination, the former interpretation will be used."* is respectfully traversed in part and overcome in part.

Applicant respectfully traverses this rejection on the basis that the specification clearly discloses who is performing the activities. As applicant teaches in paragraphs 25, 26, 68-90, and elsewhere in the specification:

"The present invention consists of a time-temperature indicator device that has at least one parameter set to warn when a therapeutic protein drug has had a thermal history associated with increased risk of unwanted immunological activity." [Paragraph 25]

"At least one of the parameters of the time-temperature indicator devices of the present invention is determined by tests for immunological stability, which is distinct from functional stability. [Paragraph 26].

This data may then be used as input into various types of time-temperature indicator, which then may be affixed to the storage container of the therapeutic protein of interest, forming a unitized device that is continually available to health care workers. [Paragraph 87]

In other words, the immunological risk data is first generated by a series of tests. Once this series of tests is complete, the time-temperature indicator device is "set" (programmed) (determined) with the test data so that it can warn users whenever the device senses immunological risk limits (as determined by this prior testing). This is taught in specification paragraph 90:

"Once the relevant time-temperature storage conditions associated with immunogenic risk have been identified, the next step in the present invention is to devise or program suitable time-temperature indicators that can warn users when an unacceptable thermal exposure has occurred." [Paragraph 90].

Applicant has respectfully overcome this rejection by amending claim 1 to incorporate a "previously" limitation to indicate that the practitioner, using experimental data, initially sets the immunological risk time-temperature indication parameters.

Applicant has further overcome this rejection by amending claim 1 with the additional limitation: *"in which said indicator output means output information pertaining to the immunological risk status of said therapeutic protein drug"* to better convey that this later step is done by the device itself.

Response to section 9:

Applicant has respectfully overcome this rejection by incorporating the transitional word "comprising" to separate the preamble from the specifications.

Response to section 10:

This rejection is respectfully traversed in part and overcome in part. Claim 5 is a dependent claim to claim 1. Claim 1, as amended, more clearly teaches that the device contains means to integrate time and temperature. Applicant respectfully traverses this rejection on the basis that claim 5 is intended to convey to the reader that some of the various types of indicator devices that can be used in the present invention are the time-temperature devices taught by the commonly owned and copending applications 10/634,297 and 10/824,709 (which subsequently issued as patents 6,950,028 and 7,102,526), the disclosures of which were incorporated into the present application by reference.

Accordingly, applicant has amended claim 5 to make it more parallel with the claim 1 limitations from the commonly owned 7,102,526 patent. Applicant respectfully requests that this amended claim 5 language be allowed as it makes the potential suitability of the 6,950,028 and 7,102,526 devices clearer to the reader.

Applicant also respectfully traverses and overcomes this rejection on the basis that claim 5 is a dependent claim to claim 1. Claim 1, as amended, now incorporates the limitations of objected-to claim 4, which examiner previously indicated is allowable if rewritten in independent form. Thus amended claim 5 now represents a further limitation to allowable claim 4.

Response to section 11:

The rejection that the limitation *"the relevant temperature" in line 4 of claim 5 has insufficient antecedent basis for this limitation"* is respectfully traversed in part and overcome in part.

As previously discussed, the specification incorporates the disclosures from patents 6,950,028 and 7,102,526 by reference. These disclosures supply the necessary

antecedent basis for "the relevant temperature". Specifically, note Column 10 lines 33-41 of patent 6,950,028:

"To obtain accurate results for most materials, the P(temp) function or lookup table should operate throughout the relevant temperature measuring range of the unit, and have a temperature granularity (ability to discriminate and generate different values for) of at least 10 degree C or smaller, and preferably 1 degree C or smaller. The time granularity, DELTA time, of the successive P(temp) measurements should be at least 1 hour or less, and should preferably be on the order of minutes or seconds." [Emphasis added].

Note also that "relevant" is used in its standard meaning, *"Having a bearing on or connection with the matter at hand"* (American Heritage Dictionary).

Applicant thus respectfully traverses this rejection on the basis that "relevant" is both adequately supported in the specification (incorporation by reference) and is also used in its nominal meaning.

As before, applicant respectfully submits that claim 5 is intended to convey to the reader that some of the various types of indicator devices that are suitable for the present invention are the time-temperature devices taught by the commonly owned and copending applications that subsequently matured into patents 6,950,028 and 7,102,526, the disclosures of which were incorporated into the present application by reference. Applicant respectfully requests that this amended claim 5 language be allowed so as to make the potential suitability of the 6,950,028 and 7,102,526 devices clearer to the reader.

Response to section 12:

The rejection that the limitation *"that periods length of time" in line 7 of claim 5 has insufficient antecedent basis for this limitation in the claim"* is respectfully traversed in part and overcome in part.

The specification incorporates the disclosures from patents 6,950,028 and 7,102,526 by reference. These disclosures supply the necessary antecedent basis for "that period's length of time." Specifically, note Column 10 lines 38-41 of 6,950,028 also teach:

The time granularity, DELTA time, of the successive P(temp) measurements should be at least 1 hour or less, and should preferably be on the order of minutes or seconds."

As before, applicant respectfully submits that, claim 5 is intended to convey to the reader that some of the various types of indicator devices that are suitable for the present invention are the time-temperature devices taught by the commonly owned and copending applications that subsequently matured into patents 6,950,028 and 7,102,526, the disclosures of which were incorporated into the present application by reference. Applicant respectfully requests that this amended claim 5 language be allowed so as to make the suitability of the 6,950,028 and 7,102,526 devices clearer to the reader.

Response to section 13:

The rejection that the language: *"contains computational means, and a temperature measurement means" can not be used to determine the equivalents of the element under 35 USC 112, sixth paragraph because there was no "function" specified before the word "means"* is respectfully overcome. As amended, claim 5 more specifically teaches that the device is an "electronic time-temperature integrator". This added "electronic time temperature integrator" limitation before the "means" clause provides the required function (i.e. electronic time-temperature integration) needed to repair the deficiency under 35 USC 112, sixth paragraph. Applicant has also amended claim 5 to be more

parallel to claim 1 from copending and commonly owned patent 7,102,526 to make the potential suitability of the 6,950,028 and 7,102,526 devices clearer to the reader.

Response to section 14:

Applicant also respectfully traverses this rejection that *"the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention."* Applicant respectfully traverses on the basis that an extensive discussion of the meaning of the terms "small enough" and "often enough" was previously provided in the specification for applicant's patents 6,950,028, and 7,102,526, the disclosures of which were both incorporated into the present specification by reference. For example, this teaching may be found in the following paragraphs from patent 6,950,028, column 9 lines 47-63:

In practice, the P(temp) value is usually produced by microprocessor algorithm that relies upon digital measurements from a temperature sensor. As a result, P(temp) usually is a step function with some granularity, such that P(temp) may produce the same results for each degree or tenth of degree of temperature. That is, for example, P(25 °C) <> P(26 °C), but P(25.02 °C) = P(25.03) °C.

Also, in practice, the successive temperature measurements are not taken infinitely close together in time, but also have some time granularity. Typically, P(temp) determinations are taken at periodic time intervals, with a typical frequency of between 1-60 minutes depending upon the application and power consumption considerations. As a result, the integral of P(temp) over time is numerically approximated by a summation function, where each element of the summation function represents the P(temp) from a different sequential time point.

As before, applicant respectfully requests that this amended claim 5 language be allowed so as to make the potential suitability of the 6,950,028 and 7,102,526 devices clearer to the reader.

Response to section 16:

The rejection of claims 6 and 13 under 35 USC 112, first paragraph as not complying with the enablement requirement is respectfully traversed in part and overcome in part. First, applicant respectfully notes that these limitations were previously discussed in more detail in specification paragraph 67:

[0067] Other types of time temperature monitor, or other environmental monitor, may also be used. As one example, if the therapeutic protein is sensitive to vibration or motion, the monitor may also have motion-sensing means. If the therapeutic protein is sensitive to light, the monitor may also have light sensing means. If the therapeutic protein forms turbidity in response to environmentally induced damage, light scattering sensing means may also be used. Typically the monitor will have at least an ability to monitor both time and a function of temperature, so as to adequately warn if the effects of temperature over time on the therapeutic protein are leading to the formation of undesirable immunological byproducts.

Applicant respectfully traverses this rejection on the grounds that electrical and other means to monitor for motion, vibration, light, or turbidity effects on proteins are extremely well known to those skilled in the art, and have been known for decades. For example, a USPTO patent search for "light scattering" and "protein" shows 4260 patents in this area. A USPTO patent search for "vibration" and "protein" shows 2249 patents in this area. A "Pub Med" search (http://www.nebi.nlm.nih.gov/entrez) of the academic literature on "light scattering" and "protein" retrieves 3600 publications spanning more than 30 years of time.

Applicant respectfully submits that given such a large number of prior art citations to draw upon, and given that these methods have been widely known for more than a generation, workers in the field would have no difficulty in selecting suitable vibration and light sensing technology.

Applicant also respectfully traverses and overcomes this rejection on the basis that amended claim 1 and 7 now incorporate the limitations of objected-to claim 4, written in independent form, and thus should be allowable. Thus claims 6 and 13, which are dependent to allowable claims 1 and 7, essentially teach further limitations on what is already allowable material based on objected-to claim 4.

Response to section 18:

The rejection of claims 1-3, 5, 7-12 as being anticipated by Karr et. al. (4,277,974) under 35 USC 102(b) is respectfully traversed in part and overcome in part. Specifically, Karr does not teach each element of independent claims 1 and 7, which is required under MPEP 2131.

According to MPEP 2131:

TO ANTICIPATE A CLAIM, THE REFERENCE MUST TEACH EVERY ELEMENT OF THE CLAIM

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is contained in the ... claim." Richardson v. Suzuki Motor Co., 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). The elements must be arranged as required by the claim, but this is not an ipsissimis verbis test, i.e., identity of terminology is not required. In re Bond, 910 F.2d 831, 15 USPQ2d 1566 (Fed. Cir. 1990). Note that, in some circumstances, it is permissible to use multiple references in a 35 U.S.C. 102 rejection. See MPEP Section 2131.01. [Emphasis added]

Applicant respectfully traverses and overcomes examiner's conclusion that *"in claims 1 and 7, the limitations listed from line 4 and line 6, respectively, to the end of the instant claims are all activities that occur outside the device."* Applicant respectfully submits

that although the test data needed to properly set the time-temperature indicator to warn of immunological risk are done externally, the results of this testing is then used to "set" the time-temperature indicator, and this setting must persist "throughout the majority of the drug's storage life" for the device to perform its intended function. Thus in order to be "set", and then to be "associated with said drug throughout the majority of the drug's storage life", and then at the end (as amended claim 1 and 7 now teach) "*output information pertaining to the immunological risk status of said therapeutic protein drug;*" some sort of lasting change in the device itself must inherently occur as a result of this testing. This change may be a lasting change in an electronic memory (e.g. the programming step taught in specification paragraph 130), or some other change.

Applicant further respectfully traverses and overcomes the 35 USC 102(b) rejection in view of Kerr on the basis that multiple limitation differences render the two inventions quite distinct from each other. Some of these differences will now be discussed.

To begin with, applicant respectfully traverses and overcomes the rejection on the basis that present claims 1 and 7, as amended, now teach monitoring an "*immunological risk status*" of a therapeutic protein drug, rather than Kerr's "*deterioration of a product that deteriorates at a rate approximately exponentially related to the temperature of the product.*

Applicant respectfully submits that the present disclosure teaches that immunological risk status is different from classic product deterioration, and also teaches that immunological risk is preferable to classic product deterioration for certain purposes (see, for example, specification figures 1 and 2, and paragraphs 37-55).

In the present specification, paragraphs 42-43, applicant teaches:

As previously discussed, as a therapeutic protein degrades, often antigenic activity may develop before the extent of degradation is large enough to produce a significant change in the therapeutic efficacy of the protein. This is because, for example, a protein

changing from a 100% monomeric state to a 95% monomeric, 5% aggregated state will typically suffer, at most, only a 5% loss in potency, which is generally too small to be observable. By contrast, the concentration of the potentially antigenic aggregates will have changed from 0% to 5% of the total amount of therapeutic protein, which is essentially an infinite increase. As a result, antigenic degradation limits will often impose more stringent time and temperature limits on a therapeutic protein's lifetime then will potency loss limits. [Emphasis added]

[0043] To avoid unwanted side effects due to antigenic activity, more stringent "antigenic generation" criteria should be used to determine the storage stability of biological therapeutics.

Note that this section is discussing "immunological risk" using alternate language commonly used in the art. The definition of "antigenic" is: *"A substance that when introduced into the body stimulates the production of an antibody...."* (American Heritage dictionary). An alternative definition is: *"A substance (usually a protein) identified as foreign by the body's immune system, triggering the release of antibodies as part of the body's immune response." (Thomson Gale dictionary).* Thus an "antigenic" therapeutic protein is an "immunological risk" therapeutic protein.

In contrast to the present disclosure, which teaches in detail how to determine immunological risk, and how distinguish it from product deterioration, Kerr totally fails to teach immunological risk, and only teaches product deterioration.

Kerr teaches that product deterioration occurs at "a *rate approximately exponentially related to the temperature of the product,"* and all of Kerr's independent claims contain this limitation. By contrast, the present disclosure teaches that immunological risk does not necessarily occur at *"a rate approximately exponentially related to the temperature of the product"* but rather may have a much more complex temperature dependency.

Something that "*deteriorates at a rate approximately exponentially related to the temperature of the product*" will deteriorate much faster at a high temperature than at a low temperature, due to the mathematics of exponential equations. It will tend to be damaged at one temperature extreme, but not the other. By contrast the present disclosure teaches something different, that immunological risk often has a "U" shaped temperature sensitivity where immunological risk can occur at <u>both</u> high and low temperatures.

For example, as shown in figures 1, 2, 4 and 5 of the present disclosure, as well as paragraphs 12, 97, 101-131 and elsewhere, many therapeutic protein drugs are damaged by <u>freezing</u>, as well as high temperature. Often, these drugs cannot be adequately modeled by the simple time-temperature indicators taught by Karr, which only teaches indicators that "*deteriorate at a rate approximately exponentially related to the temperature.*" The present art teaches the utility of using more sophisticated indicators that can incorporate exceptions to the rule that the drug deteriorates at a rate exponentially related to the temperature. See, for example, the four different temperature rules taught by the present disclosure in paragraphs 97 and paragraphs 102-105. This teaches art not contemplated by Kerr, and as a result, Kerr's "*approximately exponentially related to the temperature of the product*" limitation is not incorporated into the present claims.

Thus applicant respectfully traverses this rejection on the grounds that this element (limitation) of Kerr's claim differs from the present claims.

Applicant also respectfully traverses this rejection on the grounds that Kerr contains many other elements (limitations) that cannot be found in the present claims. In fact, most of Kerr's limitations are totally different from the present claims. Here, to emphasize this point, Kerr claim 1 is reproduced and annotated. Because Karr is so radically different from the present claims, only the aspects of Karr that are somewhat in common with the present claims are underlined. All non-underlined areas are substantially different.

1. An apparatus for indicating the deterioration of a packaged perishable product that deteriorates at a rate approximately exponentially related to the temperature of the product, the apparatus being adapted to be attached to the package in which said product is contained and comprising:

(a) a substantially planar, label-like, galvanic cell having a consumable electrode, an electrolyte, and a patterned mask positioned between said electrode and the electrolyte and protecting a predetermined portion of said electrode against galvanic erosion to provide a predetermined visual indication when the time integral of the instantaneous currents passed through said cell amounts to a predetermined coulombic total, and

(b) circuit means including a semiconductor device having a temperature dependent current characteristic connected to said cell for controlling the through-put current in a manner such that the instantaneous current amplitude at any given time is a direct and substantially exponential function of the temperature at such time, with said function substantially corresponding to the time rate of deterioration as a function of temperature characteristic of the perishable product to which the apparatus is to be attached, whereby said through-part current consumes that portion of the consumable electrode not protected by said patterned mask, exposing the electrolyte to view through said electrode and providing a visual indication corresponding to the pattern of said mask.

Even "*the deterioration*" limitation is arguably different, because as discussed, the present invention contains teaching that distinguishes between "immunological risk" and "product deterioration."

Finally, applicant respectfully overcomes the rejection on the basis that, as amended, all present claims now contain the limitations of objected-to claim 4 which, as previously discussed, were also not taught by Kerr and which examiner has indicated are allowable.

Response to Sections 19-21:

The nonstatutory obviousness-type double patenting rejection over commonly owned US patent 6,950,028 and copending application 10/824,709 (now patent 7,102,526) has been overcome by filing a terminal disclaimer to 6,950,028, enclosed with this response. Both 6,950,028 and 10/824,709 (now 7,102,526) were commonly owned by the inventor (applicant) at the time the present invention was made, and continue to be commonly owned by the inventor (applicant) as of this filing date.

Note that because the term of commonly owned patent 7,102,526 has been previously limited by terminal disclaimer also to expire on the same date as 6,950,028, a second terminal disclaimer is not necessary. All three patents (the present disclosure, 6,950,028, and 7,102,526) will expire on the same day.

Applicant respectfully traverses and overcomes examiner's rejection that "the conflicting claims are drawn to the same invention". Applicant respectfully notes that among many other differences, the present claims cover a broader variety of different types of time-temperature indictors. For example, the present art also covers chemical time-temperature indicators (exemplified by present claim 2), which were not taught by 6,950,028 and 7,102,526.

Applicant also respectfully notes that the present disclosure contains specific teaching about how to produce devices that can warn of immunological risk, which was not previously taught by 6,950,028 and 7,102,526.

New claims:

New dependent claim 20 more specifically enumerates the various output means for claim 1, and finds support in specification claim 8 and paragraphs 56 and 58. New dependent claim 23 does the same thing for new independent claim 22.

New independent claims 21 and 22 are alternate methods versions of product claim 1, and incorporate essentially the same limitations as claim 1. Thus the claims have a product-process relationship with existing claims 1-13.

In view of the above amendments and accompanying remarks, applicant believes that the application is now in condition for allowance. Notice to that effect is respectfully requested.

If the examiner believes that a telephone conference would expedite prosecution of this application, please telephone Stephen Zweig at (408) 348-1495.

Respectfully Submitted

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